

### **Remarks**

Reconsideration and reexamination of the above-identified patent application, as amended, are respectfully requested. Claims 1, 3-18, 20, 21, 23-37, 39-41, 43-57 and 59-63 are pending in the application upon entry of this Amendment. By this Amendment, the Applicant has amended claims 1, 12, 16-18, 20, 21, 32, 36, 37, 40, 41, 52, 56, 57 and 60-63. Claims 3, 23 and 43 have been canceled for consistency. No claims have been added. No new matter has been added. Of the pending claims, claims 1, 21, 41 and 61-63 are the only independent claims.

### **Specification Objections**

In the Office Action mailed December 5, 2005, the Examiner objected to the specification because it contained embedded hyperlinks and/or other forms of browser-executable code. By this paper, the specification has been amended to remove the objected to content. Consequently, Applicant believes this objection has been overcome.

### **Claim Objections**

In the Office Action mailed December 5, 2005, the Examiner objected to claim 18 under 37 C.F.R. § 1.75(c) as being of improper dependent form for failing to further limit the subject matter of a previous claim. In response to the objection, the Applicant has amended claim 18. Applicant notes that claim 18 depends directly from independent claim 1. Independent claim 1, as amended, claims calculating an equilibrium concentration for each of a plurality of species of a molecular complex in the solution at a plurality of temperatures using statistical weighing and the nucleic acid hybridization thermodynamics, wherein at least one of the plurality of species is a folded species of the molecular complex. In contrast, dependent claim 18, as amended, claims calculating a concentration of every species in a solution at a plurality of temperatures. Accordingly, Applicant respectfully contends that dependent claim 18, as amended, further limits the scope of independent claim 1, from which it depends, in that claim 18 requires calculating a concentration for every species. As a result, the objection is believed to be overcome.

**Claim Rejections - 35 U.S.C. § 112**

Claims 1, 3-18, 20, 32, 36, 37, 40, 52, 56, 57 and 60 were rejected under 35 U.S.C. § 112, second paragraph as being indefinite. Specifically, the Examiner stated that the term “best” in claims 1, 16, 17, 20, 36, 37, 40, 56, 57 and 60 is a relative term which renders the claim indefinite. Furthermore, the Examiner stated that it is unclear, with regard to claims 12, 32 and 52, what is meant by top and bottom strand sequences.

By this paper, the Applicant has amended claim 1, 20, 40 and 60 to eliminate the term “best.” Furthermore, the Applicant has amended claims 16, 17, 36, 37, 56 and 57 to clarify that the nucleic acid hybridization thermodynamics are calculated for a most thermodynamically stable target/primer or target/probe complex. Support for the modification to claims 16, 17, 36, 37, 56 and 57 may be found, for example, in the specification at page 27 lines 13-25, page 31 lines 1-5, page 32 lines 2-4, and page 33 lines 17-25. Accordingly no new matter has been added.

Also by this paper, the Applicant has amended claims 12, 32 and 52 to more particularly claim first and second strand sequences. Support for the amendment to claims 12, 32 and 52 may be found, for example, in the drawings at FIG. 2a and in the specification at page 23 lines 14-18. Accordingly, no new matter has been added.

Applicant respectfully contends that the foregoing amendments render each of claims 1, 3-18, 20, 32, 36, 37, 40, 52, 56, 57 and 60 definite under 35 U.S.C. § 112, second paragraph. Accordingly, the § 112 rejection of these claims is believed to be overcome.

**Claim Rejections - 35 U.S.C. § 103**

Claims 1, 3-5, 9-18, 20, 21, 23-25, 29-37, 39-41, 43-45, 49-57 and 59-63 were rejected under § 103(a) as being unpatentable over U.S. Patent No. 6,403,314 to Lange et al. (hereinafter “Lange”) in view of U.S. Patent No. 6,027,884 to Lane et al. (hereinafter “Lane”). Claims 6-8, 26-28 and 46-48 were rejected under § 103(a) as being unpatentable over Lange in view of Lane and further in view of Barciszewski et al., RNA Biochemistry and

Biotechnology (hereinafter "Barciszewski"). Of the rejected claims, claims 1, 21, 41 and 61-63 are the only independent claims.

Applicant believes that the claimed invention is patentable over any combination of Lange, Lane and Barciszewski and has amended independent claims 1, 21, 41 and 61-63 to more clearly define there over. In particular, Applicant has amended claims 1, 21 and 41 to more particularly claim that the correction data includes folding correction data and that the folding correction data includes a free energy value and an enthalpy value. In addition, Applicant has amended claims 1, 21 and 41 to more particularly claim calculating an equilibrium concentration for each of a plurality of species of a molecular complex in the solution at a plurality of temperatures using statistical weighing and the nucleic acid hybridization thermodynamics, wherein at least one of the plurality of species is a folded species of the molecular complex. Support for the amendments to claims 1, 21 and 41 may be found, for example, in the drawings at FIG. 1 and FIG. 2a, and in the specification at page 14 lines 19-24, page 24 lines 10-13, and page 33 lines 5-10. Accordingly, no new matter has been added.

With regard to the correction data, the Examiner relies on Lange to teach wherein the correction data includes folding correction data. *See* Office Action mailed December 5, 2005 at page 6 lines 1-2. However, those portions of Lange cited by the Examiner fail to teach or suggest the step of receiving correction data, wherein the correction data includes folding correction data and the folding correction data includes a free energy value and an enthalpy value as required by amended independent claims 1, 21 and 41.

With regard to the equilibrium concentrations, the Examiner relies on Lane to teach calculating an equilibrium concentration. *See* Office Action mailed December 5, 2005 at page 5 lines 15-22. However, rather than calculating an equilibrium concentration for each of a plurality of species wherein at least one of the plurality of species is a folded species, those portions of Lane cited by the Examiner relate to Van't Hoff plots obtained from melting data collected on the seven linear DNA fragments of FIG. 3. *See* Lane, col. 9 lines 51-55 and col.

43 lines 1-3. FIG. 3 is a list of the sequences of seven duplexes. See Lane col. 9 line 44 and FIG. 3. Accordingly, Lane does not teach or suggest calculating an equilibrium concentration for each of a plurality of species wherein at least one of the plurality of species is a folded species as presently claimed in amended independent claims 1, 21 and 41. As noted by the Examiner at page 5 lines 11-14 of the Office Action mailed December 5, 2005, Lange fails to cure this deficiency.

With regard to independent claims 61-63, the Applicant has amended these claims to more particularly claim that the correction data includes linear correction data for hybridization to DNA micro chips. Support for the modification to claims 61-63 may be found, for example, in the specification at page 23 lines 3-12. Accordingly, no new matter has been added. The Examiner relies on Lane to teach wherein the correction data includes linear correction data. See Office Action mailed December 5, 2005 at page 6 lines 3-4. However, rather than disclosing linear correction data for hybridization to DNA micro chips, those portions of Lane cited by the Examiner relate to rate measurements. See Lane col. 52 line 49. Furthermore, a review and electronic search of Lane failed to identify any occurrence of the terms "micro chip" or "chip."

For the foregoing reasons, then, neither Lane, Lange nor Barciszewski, in any order or combination, teach or suggest all the limitations of the present invention as claimed in amended independent claims 1, 21, 41 and 61-63. Accordingly, the Examiner has failed to establish a *prima facie* case of obviousness and the rejection of claims 1, 21, 41 and 61-63 should be withdrawn.

Regarding claims which depend from independent claims 1, 21, 41, 61, 62 or 63, Applicant contends that these claims are patentable for at least the same reasons that the independent claims are patentable. Moreover, Applicant contends that these claims recite further limitations, in addition to the limitations of the independent claims, which render these claims additionally patentable.

**Conclusion**

Applicant has made a genuine effort to respond to the Examiner's objections and rejections in advancing the prosecution of this case. Applicant believes all formal and substantive requirements for patentability have been met and that this case is in condition for allowance, which action is respectfully requested. Please charge any additional fees or credit any overpayments as a result of the filing of this paper to our Deposit Account No. 02-3978.

The Examiner is requested to telephone the undersigned to discuss prompt resolution of any remaining issues necessary to place this case in condition for allowance.

Respectfully submitted,  
**John SantaLucia Jr. et. al.**

By Timothy J. Marsh  
Timothy J. Marsh  
Reg. No. 56,684  
Attorney/Agent for Applicant

Date: February 22, 2006

**BROOKS KUSHMAN P.C.**  
1000 Town Center, 22nd Floor  
Southfield, MI 48075-1238  
Phone: 248-358-4400  
Fax: 248-358-3351